PATENT COOPERATION TREATY

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT 20511	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/23444	International filing date *(day/month/year)* 25 AUGUST 2000	Priority date *(day/month/year)* 30 AUGUST 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant MERCK & CO., INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12 MARCH 2001	18 SEPTEMBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Dorothea Lawrence Fox DONNA C. WORTMAN, PH.D. Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

[redacted]national application No.

PCT/US00/23444

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-26, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the claims:
pages 27-38, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the drawings:
pages 1-2, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 6, 19, 29, 41

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 6, 19, 29, 41 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/23444

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. citations and explanations (Rule 70.7)

Claims 25, 30, 31, 34, 36, 37, 42 and 43 lack novelty under PCT Article 33(2) as being anticipated by WO 97/43310. WO 97/43310 discloses HCV NS3 protease inhibitors that are based on NS4A sequences, including the peptide represented by SEQ ID NO:11, and anticipates the claimed subject matter.

Claims 1-5, 7-18, 20-24, 26-28, 32, 33, 35, 38-40, 41, 44, and 45 lack an inventive step under PCT Article 33(3) as being obvious over WO 97/43310. WO 97/43310 discloses methods for developing HCV NS3 protease inhibitors that are based on NS4A sequences and the rationale for doing so, and discloses several peptide-based protease inhibitors including the peptide represented by SEQ ID NO:11, as discussed above. It would have been obvious to one of ordinary skill in the art to make and use more, similar, HCV NS3 protease inhibitors based on NS4A sequences because WO 97/43310 establishes the interest in doing so and provides the guidance, the rationale and the methods required.

Claims 1-5, 7-18, 20-28, 30-40, and 42-45 meet the criteria for industrial applicability set out in PCT Article 33(4), because the methods and compositions are useful for the development of hepatitis C virus protease inhibitors.

---------- NEW CITATIONS ----------

WO 97/43310 A1 (SCHERING CORPORATION) 20 November 1997, see entire document, especially SEQ ID NO:11.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because:
The description does not enable practice of the invention as claimed because it presents only *in vitro*, cell-free, examples of peptide inhibition of the HCV NS2/3 protease and does not teach how to use the claimed inhibitors in an HCV infected or other cell or to treat a human patient, i.e., as a pharmaceutical, nor does it teach how to use the nucleic acid that expresses the inhibitor peptide as a pharmaceutical. While the description indicates that the intended use of the claimed compositions is as a pharmaceutical, one of skill in the art requires more than the allegation that a composition will function *in vivo* to produce a therapeutic or beneficial effect in a human patient. The description does not provide a factual basis for correlating the particular *in vitro* results presented to the *in vivo* condition as required in order to enable the claims.

Claims 1-5, 7-18, 20-24 and 34-41 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): C12Q 1/70; A61K 31/711, 38/55; C07K 14/18; C07H 21/04 and US Cl.: 435/5; 514/12, 14, 15, 44; 530/324, 327, 350; 536/ 23.72

V. 1. REASONED STATEMENTS:

The report as to Novelty was positive (YES) with respect to claims 1-5, 7-18, 20-24, 26-28, 32-40, 44, 45.
The report as to Novelty was negative (NO) with respect to claims 25, 30, 31, 34, 36, 37, 42, 43.
The report as to Inventive Step was positive (YES) with respect to claims NONE.
The report as to Inventive Step was negative (NO) with respect to claims 1-5, 7-18, 20-28, 30-40, 42-45.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-5, 7-18, 20-28, 30-40, 42-45 .
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.